1623
#5
2/22/02
NW

Dkt. 60390-G/JPW/GJG/JBC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Arlindo L. Castelhano, et al.

U.S. Serial No.: 09/728,616

Filed : December 1, 2000

For : COMPOUNDS SPECIFIC TO ADENOSINE A_3 RECEPTOR AND USES THEREOF

1185 Avenue of the Americas
New York, New York 10036
February 8, 2002

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

VOLUME 1 OF 6

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed on Form PTO-1449 **(Exhibit A)** and are also listed below. Copies of the documents listed below as items 1-112 are attached hereto as **Exhibits 1-112**, enclosed in six (6) volumes respectively.

For the convenience of the Examiner, applicants point out that references 60-63, 65-73, 75-78, 108 and 110 were cited in a corresponding PCT International Search Report for International Application No. PCT/US99/12135; reference 83 was cited in a corresponding PCT International Search Report for International Application No. PCT/US00/32702; references 79-80 were cited by the U.S. Patent Office in connection with U.S. Application No. 09/454,075; and references 109 and 111 were cited in the corresponding PCT Preliminary Examination Report for International Application No. PCT/US99/12135. A copy of the aforementioned reports can be found in Exhibits 105, 106, and 112 respectively.

1. U.S. Patent No. 5,296,484, issued March 22, 1994, Coghlan, M. J. et al. **(Exhibit 1)**;

2. U.S. Patent No. 5,409,930, issued April 25, 1995, Spada, A. P. et al. **(Exhibit 2)**;

3. U.S. Patent No. 5,516,894, issued May 14, 1996, Reppert, S. M. **(Exhibit 3)**;

4. U.S. Patent No. 5,580,870, issued December 3, 1996, Barker, A. J. et al. **(Exhibit 4)**;

5. U.S. Patent No. 5,646,130, issued July 8, 1997, Shi, G. H. **(Exhibit 5)**;

6. U.S. Patent No. 5,681,941, issued October 28, 1997, Cook, P. D. et al. **(Exhibit 6)**;

7. U.S. Patent No. 5,710,158, issued January 20, 1998, Myers, M. R. et al.**(Exhibit 7)**;

8. U.S. Patent No. 5,714,493, issued February 3, 1998, Myers, M. R. et al. **(Exhibit 8)**;

9. U.S. Patent No. 5,721,237, issued February 24, 1998, Myers, M. R. et al. **(Exhibit 9)**;

10. U.S. Patent No. 5,747,498, issued May 5, 1998, Schnur, R. C. et al. **(Exhibit 10)**;

11. U.S. Patent No. 5,780,450, issued July 14, 1998, Shade, D.

L. **(Exhibit 11)**;

12. U.S. Patent No. 5,962,458, issued October 5, 1999, Lohmann, et al. **(Exhibit 12)**;

13. PCT International Application No. WO 94/17090, published August 4, 1994 **(Exhibit 13)**;

14. PCT International Application No. WO 95/11681, published May 4, 1995 **(Exhibit 14)**;

15. PCT International Application No. WO 95/20597, published August 3, 1995 **(Exhibit 15)**;

16. PCT International Application No. WO 96/19478, published June 27, 1996 **(Exhibit 16)**;

17. PCT International Application No. WO 97/05138, published February 13, 1997 **(Exhibit 17)**;

18. PCT International Application No. WO 97/33879, published September 18, 1997 **(Exhibit 18)**;

19. PCT International Application No. WO 98/08382, published March 5, 1998 **(Exhibit 19)**;

20. PCT International Application No. WO 98/22465, published May 28, 1998 **(Exhibit 20)**;

21. PCT International Application No. WO 99/06053, published February 11, 1999 **(Exhibit 21)**;

22. PCT International Application No. WO 99/08460, published February 18, 1999 **(Exhibit 22)**;

23. PCT International Application No. WO 99/33815, published July 8, 1999 **(Exhibit 23)**;

24. PCT International Application No. WO 99/42093, published August 26, 1999 **(Exhibit 24)**;

25. European Patent Application No. EP 322 242 A2, published June 28, 1989 **(Exhibit 25)**;

26. European Patent Application No. EP 729 758 A2, published April 9, 1996 **(Exhibit 26)**;

27. Japanese Patent Application No. JP 09-291089, (English abstract only) published May 11, 1999 **(Exhibit 27)**;

28. Blazynski C., (1990) "Discrete Distributions of Adenosine Receptors in Mammalian Retina", Journal of Neurochemistry, 53: 648-655 **(Exhibit 28)**;

29. Braas K.M., et al., (1987) "Endogenous adenosine and adenosine receptors localized to ganglion cells of the retina", Proceedings of the National Academy of Science, 84: 3906-3910 **(Exhibit 29)**;

30. Bradford M. M., (1976) "A Rapid and Sensitive Method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding", Anal. Biochem., 72: 248 **(Exhibit 30)**;

31. Broach, J. R., et al., (1983) "Vectors for high level, inducible expression of cloned genes in yeast", Inouye (ed)., Experimental Manipulation of Gene Expression. Academic Press, New York, 83-117 **(Exhibit 31)**;

32. Chen, Y. L., et al., (1997) "Synthesis and Oral Efficacy of a 4-(Butylethylamino)pyrrolo[2,3-*d*]pyramidine: A Centrally Active Corticotropin-Releasing Factor$_1$ Receptor Antagonist", J. Med. Chem., 40: 1749-1754, **(Exhibit 32)**;

33. Cheng, Y. and Prusoff, W. H. (1973) "Relationship Between The Inhibition Constant (K_i) And The Concentration Of Inhibitor Which Causes 50 Per Cent Inhibition (I_{50}) Of An Enzymatic Reaction", Biochem. Pharmacol., 22: 3099-3109 **(Exhibit 33)**;

34. Christianson, T. W. et al., (1992) "Multifunctional yeast high-copy-number shuttle vectors", Gene, 110: 119-122 **(Exhibit 34)**;

35. Duzic, E. et al., (1992) "Factors Determining the Specificity of Signal Transduction by Guanine Nucleotide-binding Protein-coupled Receptors", J. Biol. Chem., 267: 9844-9851 **(Exhibit 35)**;

36. Feoktistove, I. et al., (1998) "Adenosine A_{2B} receptors: a novel therapeutic target in asthma?", TiPS 19: 148-153 **(Exhibit 36)**;

37. GenBank accession numbers S45235 and S56143 **(Exhibit 37)**;

38. GenBank accession # S46950 **(Exhibit 38)**;

39. Kang, Y. et al., (1990) "Effects of Expression of Mammalian Gα and Hybrid Mammalian-Yeast Gα Proteins on the Yeast Pheromone Response Signal Transduction Pathway", Mol. Cell. Biol., 10: 2582-2590 **(Exhibit 39)**;

40. Muller, C. E. and Stein, B. (1996) "Adenosine Receptor Antagonist: Structure and Potential Therapeutic Applications", Current Pharmaceutical Design, 2: 501-530 **(Exhibit 40)**;

41. Muller, C. E.(1997) "A_1-Adenosine Receptor Antagonists", Exp. Opin. Ther. Patents 7(5): 419-440 **(Exhibit 41)**;

42. Muller, C. E., et al., (1997) "Synthesis and Structure-Activity Relationships of 3,7-Dimethyl-1-propargylxanthine Derivatives, A_{2A}-Selective Adenosine Receptor Antagonists", J. Med. Chem., 40: 4396-4405 **(Exhibit 42)**;

43. Nyce J. W. and Metzger J. W., (1997) "DNA antisense therapy for asthma in an animal model", Nature, 385: 721-725 **(Exhibit 43)**;

44. Pichler, H. et al. (1986) "Synthese of 7-unsubstituierten 7H-Pyrrolo[2,3-d] pyrimidines", Liebigs Ann. Chemie., 9: 1485-1505 **(Exhibit 44)**;

45. Seela, F., and Lupke, U., (1977) U. Chem. Ber., 110:1462-1469 **(Exhibit 45)**;

46. Strohmeier, G. R. et al., (1995) "The A_{2b} Adenosine Receptor Mediates cAMP Responses to Adenosine Receptor Agonists in Human Intestinal Epithelia", J. Bio. Chem., 270: 2387-2394

(Exhibit 46);

47. Williams, E. F. et al., (1994) "Nucleoside transport sites in a cultured human retinal cell line established by SV-40 T antigen gene", Current Eye Research, 13: 109-118 **(Exhibit 47)**;

48. Woods, C. L. and Blazynski, C. (1991) "Characterization of Adenosine A_1-receptor Binding Sites in Bovine Retinal Membranes", Experimental Eye Research, 53: 325-331 **(Exhibit 48)**;

49. PCT International Application No. WO 99/62518, published December 9, 1999 **(Exhibit 49)**;

50. U.S. Patent No. 5,639,913, issued June 17, 1997, Lidor, R. et al. **(Exhibit 50)**;

51. U.S. Patent No. 5,834,609, issued November 10, 1998, Horne, D. A. et al. **(Exhibit 51)**;

52. U.S. Patent No. 5,877,218, issued March 2, 1999, Herzig, Y. et al. **(Exhibit 52)**;

53. U.S. Patent No. 5,877,221, issued March 2, 1999, Cohen, S. et al. **(Exhibit 53)**;

54. U.S. Patent 5,880,159, issued March 9, 1999, Herzig, Y. et al. **(Exhibit 54)**;

55. U.S. Patent No. 5,914,349, issued June 22, 1999, Cohen, S. et al. **(Exhibit 55)**;

56. U.S. Patent No. 5,994,408, issued November 30, 1999, Cohen, S. et al. **(Exhibit 56)**;

57. U.S. Patent No. 6,103,899, issued August 15, 2000, Horne, D. A. et al. **(Exhibit 57)**;

58. PCT International Application No. WO 94/24136, published October 27, 1994 **(Exhibit 58)**;

59. PCT International Application No. WO 95/18617, published July 13, 1995 **(Exhibit 59)**;

60. U.S. Patent No. 3,037,980, issued June 5, 1962, Hitchings, G. H. et al. **(Exhibit 60)**;

61. PCT International Application No. WO 93/20078, published October 14, 1993 **(Exhibit 61)**;

62. PCT International Application No. WO 94/13676, published June 23, 1994 **(Exhibit 62)**;

63. PCT International Application No. WO 95/19970, published July 27, 1995 **(Exhibit 63)**;

64. PCT International Application No. WO 98/07726, published February 26, 1998 **(Exhibit 64)**;

65. PCT International Application No. WO 98/57651, published December 23, 1998 **(Exhibit 65)**;

66. European Patent Application No. EP 0 514 540 A1, published November 25, 1992 **(Exhibit 66)**;

67. European Patent Application No. EP 0 682 027 A1, published November 15, 1995 **(Exhibit 67)**;

68. European Patent Application No. EP 0 729 758 A2, published September 4, 1996 **(Exhibit 68)**;

69. European Patent Application No. EP 0 773 023 A1, published May 14, 1997 **(Exhibit 69)**;

70. Great Britain Patent Application No. 915,303, published January 9, 1963 **(Exhibit 70)**;

71. German Patent Application No. DE 31 45 287 A1, published May 19, 1993 **(Exhibit 71)**;

72. Iwanura, H. et al. (1996) "Quantitative Aspects of the Receptor Binding of Cytokinin Agonists and Antagonists" J. Med. Chem., 26: 838-844 **(Exhibit 72)**;

73. Jorgensen, A. et al. (1985) "Synthesis of 7H-Pyrrolo[2,3-d]pyrimidin-4-amines" Liebigs, Ann. Chem., Pages 142-148 **(Exhibit 73)**;

74. Kiichiro, K. et al. "Synthesis of pyrazinecarboxylic acid derivs. - (II) derivs. of 3-aminopyrazinecarboxylic acid" (Abstract only) **(Exhibit 74)**;

75. Muller, E. C. et al. (1996) "Chiral Pyrrolo[2,3-d]pyrimidine and Pyrimido[4,5,-b]indole Derivatives: Structure-Activity Relationships of Potent, Highly Steroselective A_1-Adenosine Receptor Antaogonist" J. Med. Chem., 39: 2482-2491 **(Exhibit 75)**;

76. Muller, C. E. et al. (1990) "7-Deaza-2-phenyladenines: Structure-Activity Relationships of Potent A1 Selective Adenosine Receptor Antagonists" J. Med. Chem., 33: 2822-2828 **(Exhibit 76)**;

77. Venugopalan, B. et al. (1998) "Synthesis of 6,7-Dimethoxypyrimido[4,5-b]-indoles as Potential Antihypertensive Agents" J. Heterocyclic Chem., 25: 1663-1669 **(Exhibit 77)**;

78. West, R. A. et al. (1961) "2-Alkyl(aryl)-and 2,7-Dimethyl-4-substituted Aminopyrrolo[2,3-d]pyrimidines" J. Org. Chem., 26: 3809-3810 **(Exhibit 78)**;

79. DeNinno, M.P. in Annual Reports in Medicinal Chemistry, Vol. 33, (Academic Press: San Diego, 1998), pp. 111-120 **(Exhibit 79)**;

80. Hart, H. et al., Organic Chemistry, A Short Course, (Houghton Mifflin: 1995), p. 121 **(Exhibit 80)**;

81. U.S. Patent No. 5,646,156, issued July 8, 1997, Jacobson, et al. **(Exhibit 81)**;

82. U.S. Patent No. 5,780,481, issued July 14, 1998, Jacobson, et al. **(Exhibit 82)**;

83. U.S. Patent No. 3,910,913, issued October 7, 1975, Kim, et al. **(Exhibit 83)**;

84. PCT International Application No. WO 00-03741, published January 27, 2000 **(Exhibit 84)**;

85. Abbracchio M., et al., (1999) "Brain Adenosine Receptors as Targets for Therapeutic Intervention in Neurodegenerative Diseases", Ann. NY. Acad. Sci, 890: 79-92 **(Exhibit 85);**

86. Abbracchio M., et al., (1997) "Modulation of Apoptosis by Nervous System: a Possible Role for the A_3 Receptor", Ann. NY. Acad. Sci., 825: 11-22 **(Exhibit 86);**

87. Baraldi P., et al., (2000) "New potent and selective human adenosine A_3 receptor antagonists", Tips, 21: 456-459 **(Exhibit 87);**

88. Brand A., et al., (2001) "Adenosine A1 and A3 receptors mediate inhibition of synaptic transmission in rat cortical neurons", Neuropharmacology, 40: 85-95 **(Exhibit 88);**

89. Casavola V., et al., (1998) "Adenosine A3 receptor activation increases cystolic calcium concentration via calcium influx in A6 cells", Drug Development Research, 43 (1): 62 **(Exhibit 89);**

90. Ezeamuzie C., et al., (1999) "Adenosine A3 receptors on human eosinophils mediate inhibition of degranulation and superoxide anion release", British Journal of Pharmacology, 127: 188-194 **(Exhibit 90);**

91. Fozard J., et al., (1996) "Mast cell degranulation following adenosine A3 receptor activation in rats", European Journal of Pharmacology, 298: 293-297 **(Exhibit 91);**

92. Franco M., et al., (1999) "Adenosine Regulates Renal Nitric

Oxide Production in Hypothyroid Rats", Journal of the American Society of Nephrology, 1681-1688 **(Exhibit 92);**

93. Guerra L., et al., (1998) "Adenosine A3 receptor activation increases cytosolic calcium influx in A6 cells", Nephrology Dialysis Transplantation, 13 (6): A5 **(Exhibit 93);**

94. Jacobson K.A., et al., (1998) "Adenosine A3 receptors: novel ligands and paradoxical effects", Tips, 19:184-191 **(Exhibit 94);**

95. Jacobson K.A., et al., (1997) "Pharmacological Characterization of Novel A3 Adenosine Receptor-selective Antagonists", Neuropharmacology, 36 (9): 1157-1165 **(Exhibit 95);**

96. Lee T., et al., (2000) "Protective effects of renal ischemic preconditioning and adenosine pretreatment: role of A1 and A3 receptors", Am. J. Physiol. Renal Physiol., 278: F380-F387 **(Exhibit 96);**

97. Ohana G., et al., (2001) "Differential Effect of Adenosine on Tumor and Normal Cell Growth: Focus on the A3 Adenosine Receptor", Journal of Cellular Physiology, 186: 19-23 **(Exhibit 97);**

98. Regulation of Downstream Effectors By GPCRs, (1999) FASEB J., Abstracts 147.1-147.6 **(Exhibit 98);**

99. Reshkin J., et al., (2000) "Activation of A3 Adenosine Receptor Induces Calcium Entry and Chloride Secretion in A6 Cells", J. Membrane Biol., 178: 103-113 **(Exhibit 99);**

100. Sawynok J., et al., (1997) "Adenosine A3 receptor activation produces nociceptive behaviour and edema by release of histamine and 5-hydroxytryptamine", European Journal of Pharmacology, 333: 1-7 **(Exihibit 100);**

101. Von Lubitz, D., et al., (1999) "Chronic administration of adenosine A3 receptor agonist and cerebral ischemia: neuronal and glial effects", European Journal of Pharmacology, 367: 157-163 **(Exhibit 101);**

102. Von Lubitz D., et al., (1999) "Stimulation of Adenosine A3 Receptors in Cerebral Ischemia", Ann. NY. Acad. Sci., 890: 93-106 **(Exhibit 102);**

103. Yao Y., et al., (1997) "Adenosine A3 Receptor Agonists Protect HL-60 and U-937 Cells from Apoptosis Induced by A3 Antagonists", Biochemical And Biophysical Research Communications, 232: 317-322 **(Exhibit 103);**

104. Zhao Z., et al., (2000) "A role for the A3 Adenosine receptor in determining tissue levels of cAMP and blood pressure: studies in knock-out mice", Biochimica et Biophysica Acta, 1500: 280-290 **(Exhibit 104);**

105. International Search Report for International Application No. PCT/US99/12135 **(Exhibit 105);**

106. International Search Report for International Application No. PCT/US00/32702 **(Exhibit 106);** and

107. Lee T., et al., (1999) "Protective effects of renal ischemic preconditioning and adenosine pretreatment: role

of A1 and A3 receptors", 72nd Scientific Sessions of the American Heart Association, Atlanta, GA, p.197 **(Exhibit 107).**

108. PCT International Application No. WO 98/29397, published July 9, 1998 **(Exhibit 108)**;

109. PCT International Application No. WO 97/02266, published January 23, 1997 **(Exhibit 109)**;

110. Indian Application No. 157280, published February 22, 1986 **(Exhibit 110)**;

111. Mautner, H.G., (1961) "Potential Deoxyribonucleic Acid Cross-linking Agents. 8,8'-Bispurines", J. Org. Chem. 26(6):1914-1917 **(Exhibit 111)**; and

112. PCT International Preliminary Examination Report for International Application No. PCT/US99/12135 **(Exhibit 112)**.

Applicants request that the Examiner review the references and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Gary J. Gershik

John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in a box addressed to:
Assistant Commissioner for Patents
Washington, DC 20231

Gary J. Gershik 2/8/02

John P. White Date
Reg. No. 28,678
Gary J. Gershik
Reg. No. 39,992

8P .623

Applicant ~~Arlindo L. Castelhano, et al.~~

Client ~~OSI (1919)~~ File No. ~~60390-G~~ ~~JPW/GJG/JBC~~

Date ~~February 8, 2002~~

Kindly acknowledge receipt of the accompanying

Information Disclosure Statement in connection with Arlindo L. Castelhano, et al., COMPOUNDS SPECIFIC TO ADENOSINE A_3 RECEPTOR AND USES THEREOF U.S. Serial No. 09/728,616, filed December 1, 2000, including **Exhibit A** (Form PTO-1449), **Exhibits 1-112** and certificate of mailing dated February 8, 2002.

by placing your receiving date stamp hereon and returning to us.

COPY